LUD 5256.4 DIV (09903230)

CERTIFICATE OF FACSIMILE TRANSMITTAL

I hereby certify that this correspondence is being transmitted via telecopy pursuant to 37 CFR 1.8 to Group 1645, Examiner Jana HINES of the United States Patent & Trademark Office at (1571) 273-0859 AND (1571) 273-0864 on April 22, 2004.

Fani Malikouzakis (Name of Transmitter) Fani Malikouzakis (Signature)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Applicant	:	Ian Hiles, et al.
Serial No.	:	09/325,095
Filed	:	June 3, 1999
For	:	METHODS FOR DETERMINING EXPRESSION OF A P13 KINASE GENE
Art Unit	:	1645
Examiner	:	Jana Hines

April 22, 2004

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RESPONSE TO OFFICE ACTION
(37 C.F.R. § 1.116)

Sir:

This response is directed to the Office Action of January 27, 2004. In view of the following, a copy is being telefaxed to the Supervisory Patent Examiner.

Ab initio, applicants, believe they are entitled to an explanation for the delay in the action. Applicants filed a response, on April 9, 2003. An Office Action did not issue until **9-months later**.

Further, on April 2, 2003, applicants had a personal interview with the Examiner, and Supervisory Examiner Lynette Smith. Agreements were reached during that

interview. None are reflected in the action. Nor has the Examiner ever submitted an Examiner Interview Summary Record, as is required in these situations.

Turning now to the rejections set forth in the action, the Examiner maintains a rejection of claims 57-58, 60 and 61 as allegedly failing to satisfy the written description requirement. According to the Examiner:

> "The specification describes the hybridization method as a separate method from the PCR method, therefore there is no written description of this entire method as being capable of determining expression of the gene."

Applicants truly do not understand this statement. The polymerase chain reaction ("PCR"), is a hybridization method. It is a type of hybridization method, but not a method "separate" from hybridization.

Further, the invention does describe hybridization methodologies other than PCR, which did, in fact work. Consider, for example, page 40, line 8 - page 41, line 10. This passage describes "Southern Transfer hybridization," and "Northern Transfer hybridization." A PCR assay is described immediately after this. Hence, within a space of 2 pages, three different hybridization methodologies are describes. Clearly, there is a generic support for hybridization assays, of which PCR is an exemplary type.

Hence, this first portion of the rejection is believed improper, and should be withdrawn.

The Examiner then follows with the following statement:

> 'There is no description of an entire method that describes hybridization as a method of determining gene expression. There appears to be no support in the specification for contacting a sample with a nucleic acid molecule that hybridizes to a transcript of the gene and determines that hybridization equals to expression of the gene."

At pages 40-41, as has been stated, Southern hybridization, Northern hybridization, and PCR are described. At page 40, the Northern Transfer hybridization is carried out on "Poly(A^+)RNA," i.e., transcript.

At page 41, referring to the PCR work, "poly(A^+)RNA was reverse transcribed." In other words, transcript was reverse transcribed. It is standard practice in PCR to reverse transcribe RNA to cDNA, because the latter is more stable than the former.

Additional hybridization assays are described, at page 44, section "D," page 46, lines 9-22, page 46, line 24 - page 47, line 12, and page 52, line 18 - page 53, line 24. There are thus a plethora of examples, showing precisely what the Examiner says is absent.

The Examiner then states:

> "Moreover, the claim is drawn to a sample, however, the sample has to be RNA, since DNA cannot discriminate the transcript of the gene."

This is not correct. Northern blotting, as has been pointed out determines RNA. PCR normally uses cDNA as a template, but does not require it. It does work on RNA. It is the Examiner's burden to show it does not and the Examiner has not done so.

Further, the Examiner states that such a method is not described. Again, the Examiner should review the materials referred to *supra*.

The Examiner then goes on to argue that option (c) of claim 51 is not adequately described because it requires hybridization to the complement of SEQ ID NO: 32 or 35, and the complement is not a coding variant.

In response, applicants point out that the Examiner seems to accept that SEQ ID NOS: 32 and 35 are cDNA, and are coding variants. cDNA is a double stranded molecule. They are the coding (sense), and non-coding (antisense), strands. If the coding strand is present, the antisense strand is also present. Indeed, when PCR is carried out, primers are designed to hybridize to both strands. Please note that page 41, "PCR Determination of p85α and p110 mRNA" expressly refers to antisense and sense primers.

This is a standard assay, i.e., as is claimed, and described. The specification supports it. This aspect of the rejection is also improper.

The Examiner then states that claim 55 is not adequately described, because "there is not primer in claim 51 which would allow the polymerase chain reaction to operate."

A primer is a nucleic acid molecule which hybridizes to a target. Claim 51, lines 3-4 require "a nucleic acid molecule which hybridizes specifically to a transcript of said gene." A primer is "a nucleic acid molecule which hybridizes specifically to a transcript." With all due respect, the Examiner is wrong.

In view of the remarks presented *supra*, applicants believe that the conclusions reached by the Examiner at the end of page 4 through page 5 are incorrect, and the rejection should be withdrawn.

Turning now to the new matter rejection, the Examiner never states what the alleged new matter is. The Examiner seems to be stating that she does not accept that the described and claimed assay will *de facto* determine expression:

> "Because of the low or reduced stringency conditions of the instant claims, the method allows even distantly related genes to be identified."

The recited conditions are NOT low stringency. To the contrary, the use of, e.g., 0.1% SDS, a wash in 2xSSC, 0.1% SDS, or 0.5xSSC, 0.1% SDS, or a wash at 0.1xSSC (0.1% SDS) are very high stringency. Further, the examples identified materials which encoded the recited protein, or related proteins, NOT "distantly related genes."

If the Examiner is going to argue that a method will not work, evidence to support this is required. Pages 40-41, as has been pointed out, support the claims.

Contrary to the Examiner's statements, when an Examiner alleges non-functionality - which is what the "new matter" rejection actually does - the burden is on the Examiner to provide evidence, NOT applicants.

The Examiner then maintains that the claims lack essential steps. Hybridization *de facto* equates to expression of the gene. The conditions recited in the claims are stringent. If hybridization occurs - which is easily determined, and is shown at pages 40-41, then the expression has been determined.

Turning to the rejection at point 6, the Examiner again states that steps are missing, i.e.,

> "There is no steps for the transient expression of the product, no immuno, precipitation step..."

Neither of these is essential for a nucleic acid hybridization assay.

> "(T)here is no step which determines whether the cDNA encodes a protein with a molecular weight of 110 that possesses PI3 kinase activity."

Again, as was pointed out, *supra*, the recited conditions in the claims *de facto* lead to the recited results.

> "Finally there is no step which correlates the determination of hybridization to the determination of expression is the presence of said gene."

Applicants again direct the Examiner to the remarks made, *supra*.

All rejections to the extend they are understood, have been addressed and should be withdrawn.

APPLICANTS EXPRESSLY REQUEST AN INTERVIEW WITH SUPERVISORY EXAMINER LYNETTE SMITH IF THIS APPLICATION IS NOT ALLOWED AT THIS POINT.

Respectfully submitted,

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PAGE(S)	06
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DATE: April 22, 2004

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NUMBER OF PAGES INCLUDING COVER PAGE: 6

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RESULT	OK
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